

Status of the Claims:

- 1: previously cancelled
- 2: previously cancelled
- 3: cancelled.
- 4: previously cancelled
- 5: previously cancelled
- 6: previously cancelled
- 7: cancelled
- 8: previously cancelled
- 9: previously cancelled
- 10: cancelled

11. (Currently Amended) A recombinant nucleic acid encoding ~~the non-naturally occurring IA~~ said protein of claim ~~40~~ 35.

12. (Pending) An expression vector comprising the recombinant nucleic acid of claim 11.

13. (Pending) A host cell comprising the recombinant nucleic acid of claim 11.

14. (Pending) A host cell comprising the expression vector of claim 12.

15. (Currently Amended) A method of producing a ~~non-naturally occurring IA~~ protein having insulin activity comprising culturing the host cell of claim 13 under conditions suitable for expression of said nucleic acid.

16. (Currently Amended) ~~The~~ A method according to claim 15 further comprising recovering said IA protein.

17. (Currently Amended) A pharmaceutical composition comprising ~~an IA~~ a protein according to claim ~~40~~ 35 and a pharmaceutical carrier.

18: withdrawn

19: withdrawn

20: withdrawn

21: withdrawn

22. (Currently Amended) A ~~non-naturally-occurring IA~~ protein according to claim ~~10-35~~ wherein said ~~IA~~ protein comprises the amino acid sequence shown in ~~Figure 3A~~ (SEQ ID NO: 7).

23: withdrawn

24: withdrawn

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29: withdrawn

30: cancelled

31: cancelled

32: cancelled

33. (New) A protein having insulin activity comprising an amino acid sequence of SEQ ID NO: 2, wherein said protein has at least one substitution selected from B4-Y and B4-F.

34. (New) A protein having insulin activity comprising an amino acid sequence of SEQ ID NO: 2 wherein said protein has at least one substitution selected from the group of B5-F, B5-W, B14-F, B14-W, B14-Y, and B14-I.

35. (New) A protein having insulin activity comprising an amino acid sequence selected from the group of amino acid sequences shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, and SEQ ID NO: 23.

36. (New) A protein having occurring insulin activity comprising an amino acid sequence of SEQ ID NO: 2, wherein said protein comprises at least 2 amino acid substitutions from the A-chain and at least 5 amino acid substitutions from the B-chain and said substitutions are selected from the

group consisting of A1N, A10Q, A16Y, A17Y, A17L, A17W, A17Q, A19F, B1D, B2E, B2T, B2K, B2Q, B2D, B2R, B2N, B2F, B4Y, B4F, B4E, B4K, B4R, B8L, B8L, B8K, B8E, B11I, B12R, B12K, B14F, B14W, B14Y, B14I, B14E, B14R, B14K, B14L, B25N, B26F, B27D, B28N, and B28F.

37. (New) A protein according to claim 30, wherein said substitutions are selected from the group consisting of A1-N, A10-Q, A16-Y, A17-Y, A19-F, B1-D, B2-K, B4-F, B8-L, B11-I, B12-R, B14-W, B25-N, B26-F, B27-D, and B28-N.

38. (New) A recombinant nucleic acid encoding the non-naturally occurring IA protein selected from the group consisting of: SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, and SEQ ID NO: 23.